REMARKS

Restriction: The Examiner requires restriction to one of the following inventions:

Group I: including claim(s) 1-13, drawn to pharmaceutical compositions comprising at least one tetrahydrofolate, methylene-tetrahydrofolate, and methyl-tetrahydrofolate and at least one multi-targeting antifolate; or

Group II: including claim(s) 1-7 and 17-23, drawn to methods of treating cancer comprising administering at least one tetrahydrofolate, methylene-tetrahydrofolate, and methyl-tetrahydrofolate and at least one multi-targeting antifolate; or

Group III: including claim(s) 1-7, drawn to methods of manufacturing a composition comprising administering at least one tetrahydrofolate, methylene-tetrahydrofolate, and methyl-tetrahydrofolate and at least one multi-targeting antifolate; or

Group IV: including claim(s) 14-16, drawn to kits comprising a pharmaceutical composition comprising at least one tetrahydrofolate, methylene-tetrahydrofolate, and methyl-tetrahydrofolate and at least one multi-targeting antifolate.

In accordance with the Examiner's grouping of claims, Applicants respectfully submit that Group I would actually comprise claims 8-13, rather than claims 1-13, and Group II would only comprise claims 17-23. Therefore, Applicants elect the following group, ***with*** traverse:

Group I: including claim(s) 8-13, drawn to pharmaceutical compositions comprising at least one tetrahydrofolate, methylene-tetrahydrofolate, and methyl-tetrahydrofolate and at least one multi-targeting antifolate.

Species: The Examiner further requires an election of one of the following species for prosecution in this application:

The multitude of structurally diverse compounds encompassed by the genus "multi-targeting antifolate" as recited in claims 1, 8, 14 and 17.

Therefore, Applicants elect the following species, ***with*** traverse: pemetrexed.

Arguments in Support of Traversal

The Examiner asserts that Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the claimed tetrahydrofolate, methylene-tetrahydrofolate, and methyl-tetrahydrofolate and multi-targeting antifolates were knowin in the art at the time the invention was made know as evidenced by the references cited in Applicant's disclosure, and thus are not a special technical feature linking the claimed inventions, combining methylene-tetrahydrofolate with an antifolate was known in the art as evidenced by WO 91/17660.

Applicant recognizes that whether or not any particular technical feature makes a contribution over the prior art, and therefore constitutes a "*special technical feature*" may be considered with respect to novelty and inventive step. That is, the Examiner may consider the prior art in making his Unity of Invention determination. In this case, however, the Examiner has not provided any comments whatsoever as to how WO 91/17660 teaches or suggests each and

every feature of the invention defined by the claims of Groups I-IV or the species election of compounds encompassed by the genus "multi-targeting antifolate" as recited in claims 1, 8, 14 and 17. Without this information, Applicants cannot properly respond to the Restriction Requirement, and as a result, the basis for the Restriction Requirement is incomplete. If the Examiner maintains the Restriction Requirement, then he should at least point out (by column and line) how the asserted reference meets each and every feature of the invention defined by the claims of Groups I-IV and the aforementioned species.

Furthermore, Applicant respectfully submits that the present invention is linked by the special technical feature of combining tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate with a ***multi-targeting*** antifolate (i.e. an antifolate acting on ***two or more*** of the enzymes involved in folate synthesis; see page 14, lines 24-27 of the specification as filed). In contrast, WO 91/17660 discloses a combination of methylene-tetrahydrofolate and a single-targeting antifolate (i.e. an antifolate acting on a single enzyme). In addition, the species of pemetrexed, raltitrexed and lometerexol share the feature of being ***multi-targeting*** (i.e. acting on ***two or more*** of the enzymes involved in folate synthesis; see page 14, lines 24-27 of the specification as filed).

Further, upon the allowance of a claim with a "*special technical feature*" and/or allowance of a generic claim, Applicant respectfully requests rejoinder of

all claims containing that "*special technical feature*" and/or all claims dependent on that generic claim.

CONCLUSION

For all of the above stated reasons, reconsideration and withdrawal of the outstanding restriction/election requirement and favorable allowance of all claims in the instant application are earnestly solicited.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

HARNESS, DICKEY & PIERCE, PLC

By Eric G. Hoffman Reg. No. 57752
Donald J. Daley, Reg. No. 34,313
P.O. Box 8910
Reston, VA 20195
(703) 668-8000

DJD/EGH/dmc